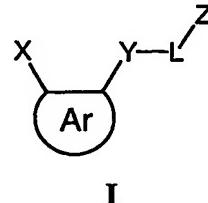


What is claimed is:

1. A compound for modulating kinase activity of Formula I,



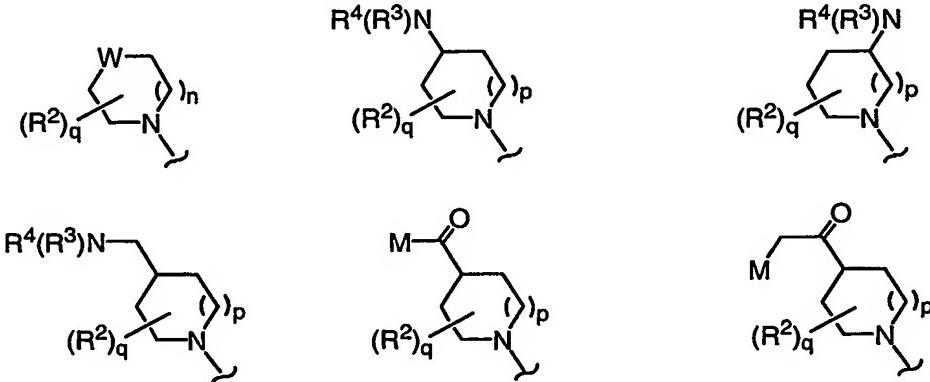
or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

Ar is a five- to six-membered aromatic ring system containing between one and three heteroatoms, said five- to six-membered aromatic ring system substituted with -X and -Y-L-Z, in an ortho relationship to each other, and said five- to six-membered aromatic ring system optionally substituted with up to four R¹;

each R¹ is independently selected from -H, halogen, -CN, -NO₂, -OR³, -N(R³)R³, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, -OC(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocycl, and optionally substituted lower heterocyclalkyl;

optionally two of R¹, together with the atoms to which they are attached, form a first ring system fused with Ar, said first ring system substituted with zero to three additional of R¹;

X is selected from the following six formulae:



wherein,

W is selected from -C(R²)(R²)-, -N(R⁴)-, -S(O)₀₋₂-, and -O-;

n = 1 or 2;

p = 0 or 1;

q is 1 to 3;

M is -OR³ or -N(R³)R⁴;

each R² is independently selected from -H, halogen, oxo, -CN, -NH₂, -NO₂, -OR³, -N(R³)R³, -N(R³)R⁵, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -N(R³)C(O)N(R³)R³, -C(O)R³, -OC(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

two of R², together with the atoms to which they are attached, can form an optionally substituted three- to seven-membered ring system;

each R³ is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; or

two of R³, when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P;

each R⁴ is independently selected from R³, -SO₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, and -C(O)R³;

Y is selected from -CH₂- , -O- , -S(O)₀₋₂- , -N(R³)- , and absent;

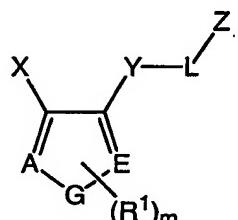
L is selected from -(CH₂)₁₋₃- , -(CH₂)₁₋₃N(R³)- , -(CH₂)₁₋₃O- , -(CH₂)₁₋₃S(O)₀₋₂- and absent; each of the aforementioned methylenes optionally substituted;

Z is a five- to seven-membered ring system or -R³, said five- to seven-membered ring system optionally substituted with zero to four of R⁵; and

R⁵ is selected from -H, halogen, -CN, oxo, -NO₂, -OR³, -N(R³)R⁴, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl; and

optionally two of R⁵, together with the atoms to which they are attached, form a second ring system fused with said five- to seven-membered ring system, said second ring system substituted with zero to four of R⁵.

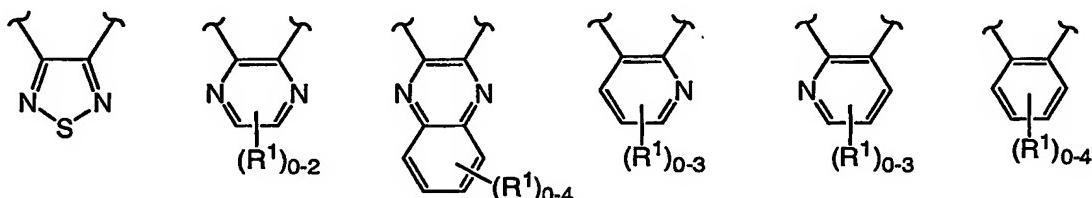
2. The compound according to claim 1, of formula II,



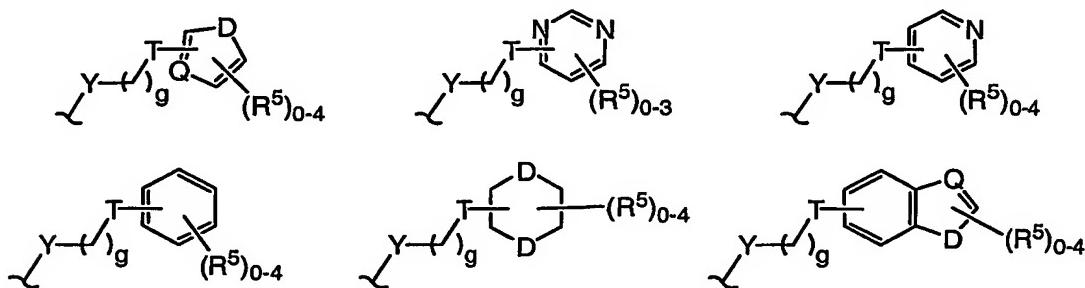
II

wherein, A and E are each independently N or -C(R¹)-; and G is selected from -S(O)₀₋₂- and -C(R¹)=C(R¹)-.

3. The compound according to claim 2, wherein Ar is selected from the following formulae.



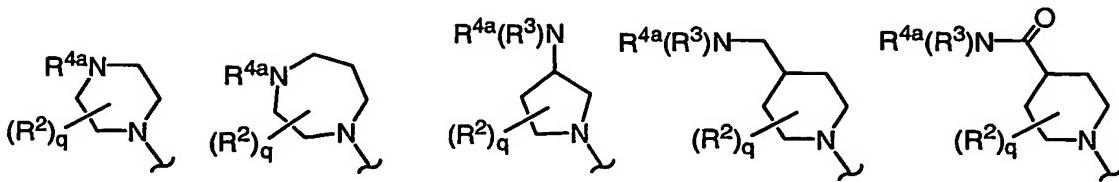
4. The compound according to claim 3, wherein -Y-L-Z is selected from the following formulae,



wherein g is zero to two; D is selected from -C(R⁵)(R⁵)-, -O-, -S(O)₀₋₂-, and -N(R⁴)-; Q is =N- or -C(R⁵)-, T is selected from absent, -N(R³)-, -S- and -O-; and each methylene between Y and T is optionally substituted; provided that when both Y and T are heteroatoms then g must be two.

5. The compound according to claim 4, wherein Y is -O- or optionally substituted -CH₂-.

6. The compound according to claim 5, wherein X is selected from the following formulae.



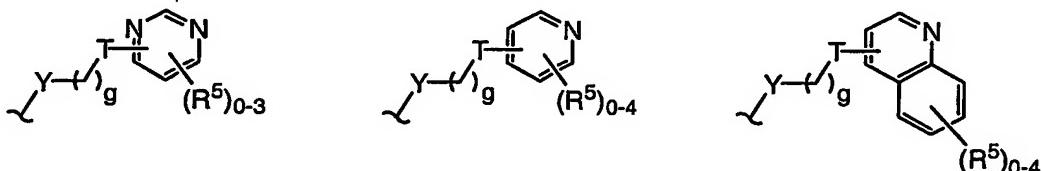
7. The compound according to claim 6, wherein R^{4a} is selected from -SO₂R³, -SO₂N(R³)R⁴, -CO₂R³, -C(O)N(R³)R⁴, and -C(O)R³.

8. The compound according to claim 7, wherein each R² is independently selected from -H or optionally substituted lower alkyl.

9. The compound according to claim 8, wherein each R² is independently selected from -H, haloalkyl, -C₁₋₆alkyl-N(R³)R³, -C₁₋₆alkyl-OR³, -C₁₋₆alkyl-CO₂R³, and -C₁₋₆alkyl-C(O)N(R³)R³.

10. The compound according to claim 9, wherein R^{4a} is -C(O)N(R³)R³ or -C(O)R³.

11. The compound according to claim 10, wherein -Y-L-Z is selected from the following formulae,

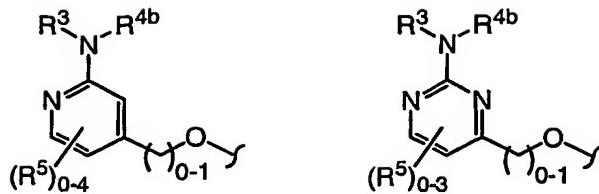


wherein Y, T, and g are as described above.

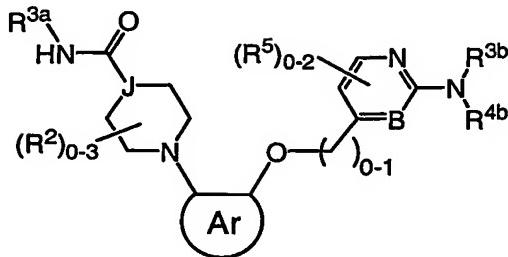
12. The compound according to claim 11, wherein g is one or two.

13. The compound according to claim 12, wherein each R⁵ is independently selected from -H, halogen, -CN, -NH₂, -NO₂, -OR³, -N(R³)R⁴, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, and optionally substituted lower alkyl.

14. The compound according to claim 13, wherein -Y-L-Z is selected from the following formulae.



15. The compound according to claim 14, having formula III,



III

wherein J is N or CH, and B is =N- or =C(R⁵)-.

16. The compound according to claim 15, wherein R^{3a} is selected from optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl.

17. The compound according to claim 16, wherein R^{3a} is selected from optionally substituted aryl and optionally substituted heteroaryl.

18. The compound according to claim 17, wherein R^{3a} is optionally substituted phenyl.

19. The compound according to claim 18, wherein said optionally substituted phenyl is substituted with at least one of halogen, -CN, -CF₃, -NH₂, -NO₂, -OR³, -N(R³)R³, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted lower alkyl, and optionally substituted aryl.

20. The compound according to claim 19, wherein said optionally substituted phenyl group is substituted with at least one trifluoromethyl group.

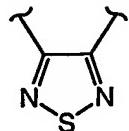
21. The compound according to claim 20, wherein said optionally substituted phenyl group is substituted with at least two trifluoromethyl groups

22. The compound according to claim 19, wherein said optionally substituted phenyl group is substituted with at least one lower alkyl group.

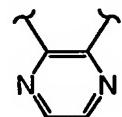
23. The compound according to claim 19, wherein R^{3b} is -H.

24. The compound according to claim 23, wherein R^{4b} is selected from R³, -H, -CO₂R³, -C(O)N(R³)R⁴, and -C(O)R³.

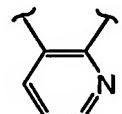
25. The compound according to claim 24, wherein Ar is according to the formula below.



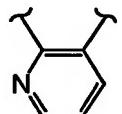
26. The compound according to claim 24, wherein Ar is according to the formula below.



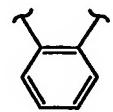
27. The compound according to claim 24, wherein Ar is according to the formula below.



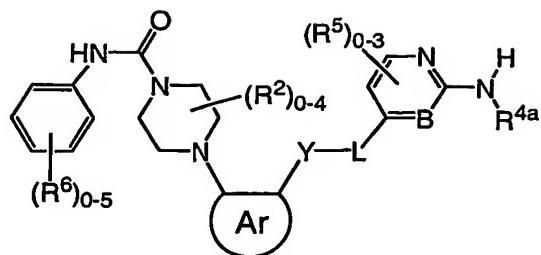
28. The compound according to claim 24, wherein Ar is according to the formula below.



29. The compound according to claim 24, wherein Ar is according to the formula below.

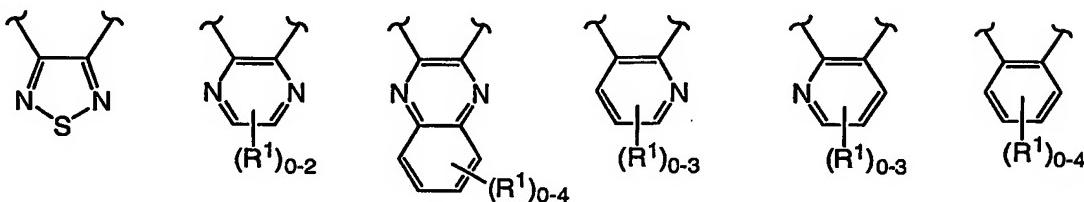


30. A compound for modulating kinase activity of Formula IV,

**IV**

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

Ar is selected from the following formulae:



each R¹ is independently selected from -H, halogen, -CN, -NO₂, -OR³, -N(R³)R³, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl;

optionally two of R¹, together with the atoms to which they are attached, form a first ring system fused with Ar, said first ring system substituted with zero to three additional of R¹;

each R² is independently selected from -H, halogen, oxo, -CN, -NH₂, -NO₂, -OR³, -N(R³)R³, -N(R³)R⁵, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -N(R³)C(O)N(R³)R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl;

two of R², together with the atoms to which they are attached, can form an optionally substituted three- to seven-membered ring system;

each R³ is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl; or

two of R³, when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl ring, said optionally

substituted five- to seven-membered heterocyclyl ring optionally containing at least one additional heteroatom selected from N, O, S, and P;

each R⁴ is independently selected from R³, -SO₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R³, and -C(O)R³;

Y is selected from optionally substituted -CH₂- , -O-, -S-, and -N(R³)-;

L is selected from optionally substituted -CH₂- , -O-, -S-, -N(R³)- and absent;

provided that Y and L are not both heteroatoms;

B is =N- or =C(H)-;

at each instance, R⁵ and R⁶ are independently selected from -H, halogen, -CN, -NO₂, -OR³, -N(R³)R⁴, -S(O)₀₋₂R³, -SO₂N(R³)R³, -CO₂R³, -C(O)N(R³)R, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclalkyl; and

optionally two of R⁵, together with the atoms to which they are attached, form a ring system fused with the ring containing B according to formula IV, said ring system substituted with zero to two additional of R⁵.

31. The compound according to claim 30, wherein Y is -O- and L is optionally substituted -CH₂-.

32. The compound according to claim 31, wherein at least one of R⁶ is optionally substituted lower alkyl.

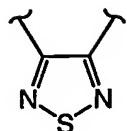
33. The compound according to claim 32, wherein said at least one optionally substituted lower alkyl is *meta*- to the piperazine urea function as depicted in formula IV.

34. The compound according to claim 33, wherein R^{4a} is selected from R³, -H, -CO₂R³, -C(O)N(R³)R⁴, and -C(O)R³.

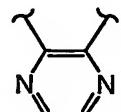
35. The compound according to claim 34, wherein R^{4a} is selected from -H, -CO₂R³, -C(O)N(R³)R⁴, and -C(O)R³.

36. The compound according to claim 35, wherein -Y-L- is -OCH₂-.

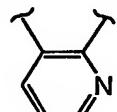
37. The compound according to claim 36, wherein Ar is according to the formula below.



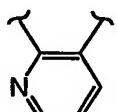
38. The compound according to claim 36, wherein Ar is according to the formula below.



39. The compound according to claim 36, wherein Ar is according to the formula below.



40. The compound according to claim 36, wherein Ar is according to the formula below.



41. The compound according to claim 36, wherein Ar is according to the formula below.



42. The compound according to claim 1, selected from Table 4.

Table 4

1	N-[(1 <i>R</i> ,2 <i>S</i>)-2-phenylcyclopropyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
2	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	

Table 4

3	N-[4-chloro-3-(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
4	N-[4-(1-methylethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
5	N-(3-bromophenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
6	N-[3-(methylthio)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
7	N-(3-ethylphenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
8	N-(3,5-dimethylphenyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
9	N-[3-trifluoromethylphenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	

Table 4

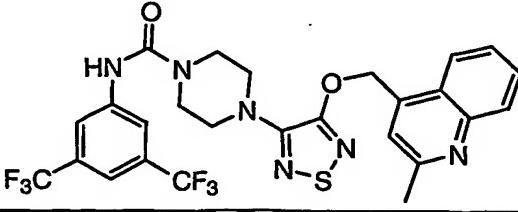
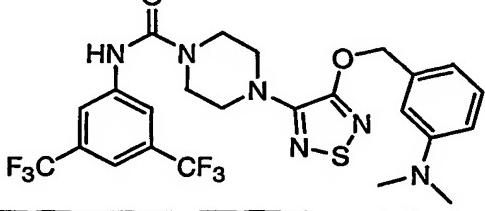
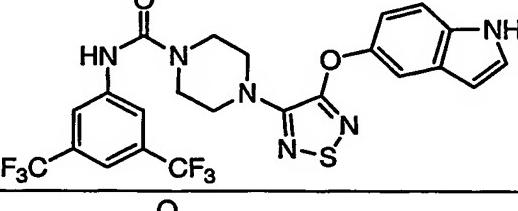
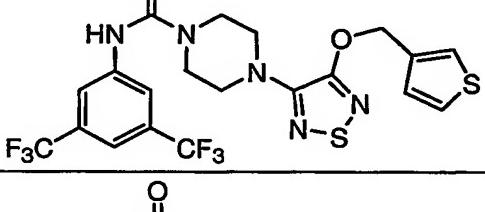
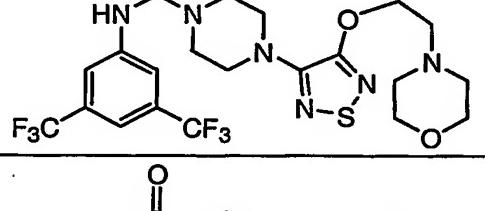
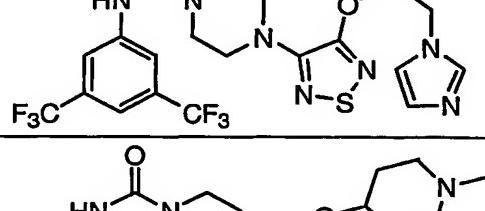
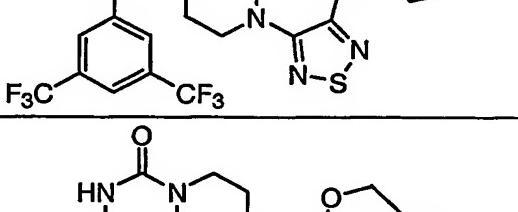
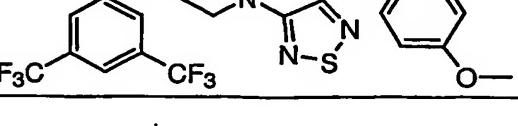
10	N-[3,5-bis(trifluoromethyl)phenyl]-4-{[(2-methylquinolin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
11	N-[3,5-bis(trifluoromethyl)phenyl]-4-{[(3-dimethylamino)phenyl]methyl}oxy)-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
12	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-(1H-indol-5-yloxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
13	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(3-thienyl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
14	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-morpholin-4-ylethyl)oxy]-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
15	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-(1H-imidazol-1-yl)ethyl)oxy]-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
16	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(1-methylpiperidin-4-yl)oxy]-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
17	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(4-methoxyphenyl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	

Table 4

18	4-[4-({[3,4-bis(methoxy)phenyl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
19	4-{4-[(1,3-benzodioxol-5-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
20	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(furan-3-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
21	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(tetrahydrofuran-3-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
22	N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
23	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-1,4-diazepane-1-carboxamide	
24	1-({[(1S,2R,5S)-5-methyl-2-(1-methylethyl)cyclohexyl]oxy}acetyl)-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl)piperazine	
25	5-phenyl-N-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)-1,3-oxazole-4-carboxamide	

Table 4

26	1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-4-{[3-(trifluoromethyl)phenyl]acetyl}piperazine	
27	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(piperidin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
28	N-[3,5-bis(trifluoromethyl)phenyl]-N'-(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperidin-4-yl)methylurea	
29	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(3-pyridin-3-ylpropyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
30	N-[3,5-bis(trifluoromethyl)phenyl]-4-{1,1-dioxido-4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
31	4-[4-(1-azabicyclo[2.2.2]oct-3-yloxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
32	4-[(4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl)oxy)methyl]benzoic acid	

Table 4

33	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(piperidin-3-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
34	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-pyrrolidin-1-ylethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
35	4-{4-[(2-amino-2-methylpropyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
36	N-[3,5-bis(trifluoromethyl)phenyl]-1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperidine-4-carboxamide	
37	1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperidine-4-carboxamide	
38	N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
39	4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
40	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-piperidin-4-ylethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	

Table 4

41	2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
42	1-phenyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	
43	1-[(4-methylphenyl)methyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	
44	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)amino]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
45	4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]-1,4-diazepane-1-carboxamide	
46	2-methyl-1-[[2-(methyoxy)phenyl]carbonyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	
47	N-[5-chloro-2-(methyoxy)phenyl]-N'-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)urea	

Table 4

48	N-[5-methyl-2-(methyloxy)phenyl]-N'-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)urea	
49	N-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)-N'-(3-(trifluoromethyl)phenyl)urea	
50	2-methyl-N-[4-(1-methylethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
51	2-methyl-N-[3-(methylthio)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
52	(2R)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
53	(2R)-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
54	1-[4-(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazin-1-yl)phenyl]ethanone	

Table 4

55	2-(4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazin-1-yl)pyrimidine	
56	1-[2-nitro-4-(trifluoromethyl)phenyl]-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	
57	(2S)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
58	(2S)-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
59	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-hydroxypyrazin-2-yl)piperazine-1-carboxamide	
60	2-[2,5-bis(trifluoromethyl)phenyl]-N-(1-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}pyrrolidin-3-yl)acetamide	
61	1-{[2,5-bis(trifluoromethyl)phenyl]acetyl}-2-methyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine	

Table 4

62	N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
63	2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
64	N-[3,5-bis(trifluoromethyl)phenyl]-2,6-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
65	2,6-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
66	N-(1-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}pyrrolidin-3-yl)-N'-[3-(trifluoromethyl)phenyl]urea	
67	N-[3,5-bis(trifluoromethyl)phenyl]-N'-(1-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}pyrrolidin-3-yl)urea	
68	N-[3,5-bis(trifluoromethyl)phenyl]-2,6-dimethyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	

Table 4

69	2,6-dimethyl-4-{4-[(pyridin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
70	N-[3,5-bis(trifluoromethyl)phenyl]-3-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
71	3-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
72	N-[3,5-bis(trifluoromethyl)phenyl]-4-{2-[(pyridin-4-ylmethyl)oxy]phenyl}piperazine-1-carboxamide	
73	4-{2-[(pyridin-4-ylmethyl)oxy]phenyl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
74	N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]quinoxalin-2-yl}piperazine-1-carboxamide	
75	N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-1,4-diazepane-1-carboxamide	

Table 4

76	2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]quinoxalin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
77	4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]-1,4-diazepane-1-carboxamide	
78	N-[3,5-bis(trifluoromethyl)phenyl]-2,5-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
79	2,5-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
80	(2S)-N-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
81	(2S)-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
82	N-[3,5-bis(trifluoromethyl)phenyl]-4-{[(2-fluoropyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	

Table 4

83	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-[(2-chloropyridin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
84	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-[(2-chloropyridin-4-yl)methyl]oxy)pyrazin-2-yl)piperazine-1-carboxamide	
85	N-[3,5-bis(trifluoromethyl)phenyl]-4-(2-[(2,3,5,6-tetrafluoropyridin-4-yl)amino]methyl)phenyl)piperazine-1-carboxamide	
86	N-[3,5-bis(trifluoromethyl)phenyl]-4-(2-[(3-chloro-2,5,6-trifluoropyridin-4-yl)amino]methyl)phenyl)piperazine-1-carboxamide	
87	N-[3,5-bis(trifluoromethyl)phenyl]-4-(4-[(2-bromopyridin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
88	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-[(2-bromopyridin-4-yl)methyl]oxy)pyrazin-2-yl)piperazine-1-carboxamide	

Table 4

89	N-[3,5-bis(trifluoromethyl)phenyl]-4-(3-[(2-fluoropyridin-4-yl)methyl]oxy)pyrazin-2-yl)piperazine-1-carboxamide	
90	N-[3,5-bis(trifluoromethyl)phenyl]-4-{5,6-dicyano-3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
91	4-{5,6-dicyano-3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}-N-[3-(trifluoromethyl)phenyl)piperazine-1-carboxamide	
92	N-(3-ethylphenyl)-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
93	N-(3-ethylphenyl)-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	
94	N-(3-ethylphenyl)-2,6-dimethyl-4-{3-[(pyridin-4-ylmethyl)oxy]pyrazin-2-yl}piperazine-1-carboxamide	

Table 4

95	N-(3-ethylphenyl)-2-methyl-4-{3-[(pyridin-4-ylmethyl)oxy]quinoxalin-2-yl}piperazine-1-carboxamide	
96	N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-(2-pyridin-4-ylethyl)pyrazin-2-yl}piperazine-1-carboxamide	
97	N-[3,5-bis(trifluoromethyl)phenyl]-4-{3-[(pyridin-4-ylmethyl)oxy]pyridin-2-yl}piperazine-1-carboxamide	
98	N-[3,5-bis(trifluoromethyl)phenyl]-4-{2-[(pyridin-4-yloxy)methyl]phenyl}piperazine-1-carboxamide	
99	4-(4-{{(2-aminopyridin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl)piperazine-1-carboxamide	
100	1,1-dimethylethyl {4-[({4-[{4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	

Table 4

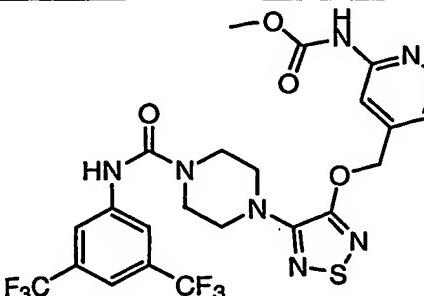
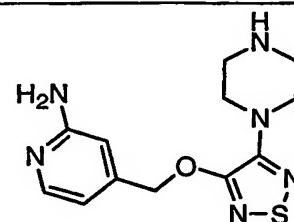
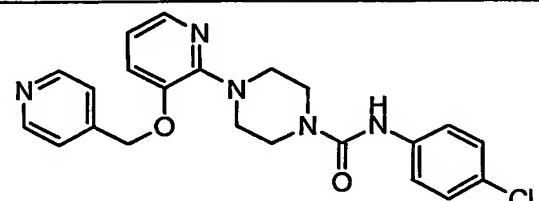
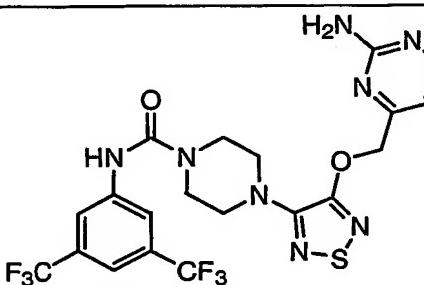
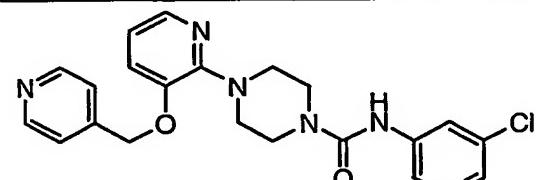
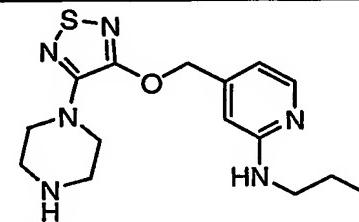
101	methyl {4-[{4-[{4-((3,5-bis(trifluoromethyl)phenyl)amino)carbo- nyl)piperazin-1-yl]-1,2,5-thiadiazol-3- yl}oxy)methyl}pyridin-2-yl carbamate	
102	4-{[(4-piperazin-1-yl)-1,2,5-thiadiazol-3- yl]oxy}methyl}pyridin-2-amine	
103	N-(4-chlorophenyl)-4-{3-[(pyridin-4- ylmethyl)oxy]pyridin-2-yl}piperazine- 1-carboxamide	
104	4-(4-{[(2-aminopyrimidin-4- yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)- N-[3,5- bis(trifluoromethyl)phenyl]piperazine-1- carboxamide	
105	N-(3-chlorophenyl)-4-{3-[(pyridin-4- ylmethyl)oxy]pyridin-2-yl}piperazine- 1-carboxamide	
106	4-{[(4-piperazin-1-yl)-1,2,5-thiadiazol-3- yl]oxy}methyl}-N-propylpyridin-2- amine	

Table 4

107	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(propylamino)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
108	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(methylamino)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
109	N-methyl-4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	
110	N-ethyl-4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	
111	N-butyl-4-{[(4-piperazin-1-yl-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-amine	
112	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(methylamino)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	

Table 4

113	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(ethylamino)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
114	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(butylamino)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
115	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-[(2-[(phenylmethyl)amino]pyridin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
116	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-[(2-[(1-methylethyl)amino]pyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
117	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-[(2-[(phenylmethyl)amino]pyrimidin-4-yl)methyl]oxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	

Table 4

118	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(phenylamino)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
119	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-{{(2-{[2-(dimethylamino)ethyl]amino}pyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
120	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-{{(2-{[2-(dimethylamino)ethyl]amino}pyridin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
121	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(ethylamino)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
122	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(propylamino)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	

Table 4

123	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-((2-(cyclopropylamino)pyrimidin-4-yl)methyl)oxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
124	4-[4-((2-(acetylamino)pyrimidin-4-yl)methyl)oxy]-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
125	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-((2-[(phenylcarbonyl)amino]pyridin-4-yl)methyl)oxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
126	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-((2-[(phenylcarbonyl)amino]pyrimidin-4-yl)methyl)oxy]-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
127	4-[4-((2-[bis(phenylcarbonyl)amino]pyridin-4-yl)methyl)oxy]-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	

Table 4

128	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(cyclopentylamino)pyrimidin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
129	4-[4-({[2-(acetylamino)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
130	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-[{[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl]amino}pyridin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
131	methyl {4-[({4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl}carbamate	
132	4-(4-[(2-aminopyridin-4-yl)methyl]oxy)-1,2,5-thiadiazol-3-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	

Table 4

133	methyl [4-({[4-({[(3-ethylphenyl)amino]carbonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyridin-2-yl]carbamate	
134	N-[3,5-bis(trifluoromethyl)phenyl]-4-{{[(2-cyanopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
135	4-(3-{{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
136	4-[[{4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl]pyrimidine-2-carboxamide	
137	N-[3,5-bis(trifluoromethyl)phenyl]-4-{{[(2-butyloxy)pyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	

Table 4

138	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(pyrimidin-4-ylmethyl)oxy]-1,2,5-thiadiazol-3-yl}piperazine-1-carboxamide	
139	4-[(4-[(4-((3,5-bis(trifluoromethyl)phenyl)amino)carbo-nyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl)oxy]methyl]pyridine-2-carboxylic acid	
140	2-pyrrolidin-1-ylethyl {4-[(4-[(4-((3,5-bis(trifluoromethyl)phenyl)amino)carbo-nyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-yl carbamate	
141	2-morpholin-4-ylethyl {4-[(4-[(4-((3,5-bis(trifluoromethyl)phenyl)amino)carbo-nyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-yl carbamate	
142	4-(3-[(2-aminopyrimidin-4-yl)methyl]oxy)pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	

Table 4

143	N-[3,5-bis(trifluoromethyl)phenyl]-4-[(2-{[(1-methylpiperidin-3-yl)carbonyl]amino}pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
144	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
145	2-(4-methylpiperazin-1-yl)ethyl {4-[(4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl)oxy]methyl}pyridin-2-yl carbamate	
146	N-[3,5-bis(trifluoromethyl)phenyl]-4-[(2-{[(1-ethylpiperidin-4-yl)carbonyl]amino}pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
147	4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-{3-[(trifluoromethyl)thio]phenyl}piperazine-1-carboxamide	

Table 4

148	4-({[4-(4-{[3,5-bis(trifluoromethyl)phenyl]sulfonyl}piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyridin-2-amine	
149	4-(4-{[(2-aminopyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-naphthalen-1-ylpiperazine-1-carboxamide	
150	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(N,N-dimethylglycyl)amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
151	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(morpholin-4-ylacetyl)amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
152	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[(2-[(piperidin-1-ylacetyl)amino]pyridin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	

Table 4

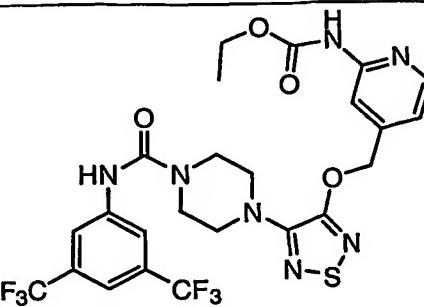
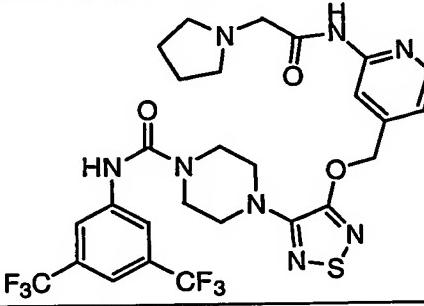
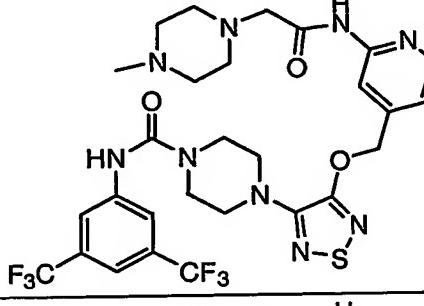
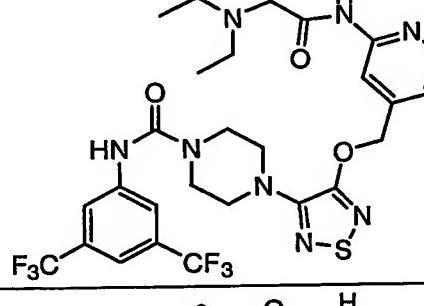
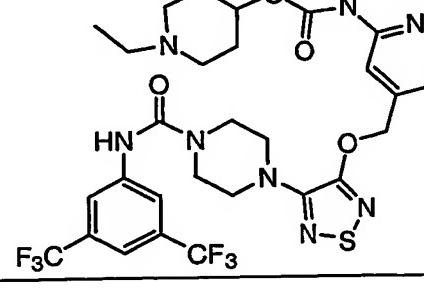
153	ethyl {4-[{4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	
154	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[{2-[(pyrrolidin-1-yl)acetyl]amino}pyridin-4-yl]methyl}oxy]-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
155	N-[3,5-bis(trifluoromethyl)phenyl]-4-{[(2-[(4-methylpiperazin-1-yl)acetyl]amino)pyridin-4-yl]methyl}oxy]-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
156	N-[3,5-bis(trifluoromethyl)phenyl]-4-{4-[{2-[(N,N-diethylglycyl)amino}pyridin-4-yl]methyl}oxy]-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
157	1-ethylpiperidin-4-yl {4-[{4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	

Table 4

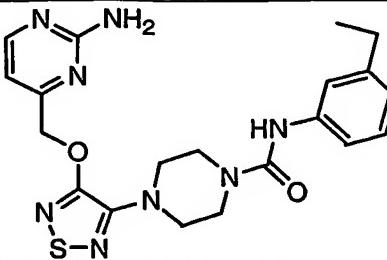
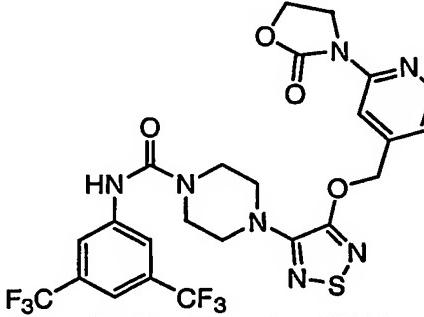
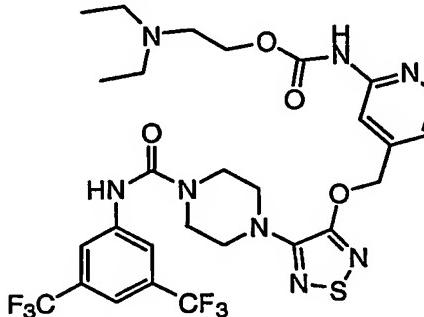
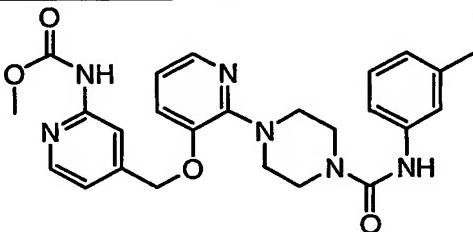
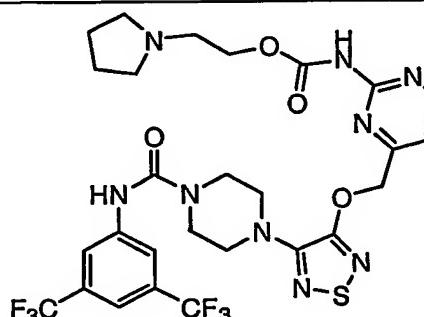
158	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
159	N-[3,5-bis(trifluoromethyl)phenyl]-4-[4-({[2-(2-oxo-1,3-oxazolidin-3-yl)pyridin-4-yl]methyl}oxy)-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
160	2-(diethylamino)ethyl {4-[{4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyridin-2-yl}carbamate	
161	methyl [4-({[2-(4-{[(3-ethylphenyl)amino]carbonyl}piperazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]carbamate	
162	2-pyrrolidin-1-ylethyl {4-[{4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl}carbamate	

Table 4

163	2-piperidin-1-ylethyl {4-[{(4-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-yl}carbamate	
164	methyl [4-{[2-(4-{[(3-bromophenyl)amino]carbonyl}piperazin-1-yl)pyridin-3-yl]oxy}methyl]pyridin-2-yl]carbamate	
165	methyl {4-[{(2-[4-({[3-(methyloxy)phenyl]amino}carbonyl)piperazin-1-yl]pyridin-3-yl}oxy)methyl]pyridin-2-yl}carbamate	
166	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(methyloxy)phenyl]piperazine-1-carboxamide	
167	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide	
168	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-((trifluoromethyl)oxy)phenyl]piperazine-1-carboxamide	
169	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	

Table 4

170	N-(3-ethylphenyl)-4-[3-{[2-{[(3-ethylphenyl)amino]carbonyl}amino]pyridin-4-yl}methyl]oxy]pyridin-2-yl]piperazine-1-carboxamide	
171	N-(3-ethylphenyl)-4-[3-{[(2-{[(4-methylpiperazin-1-yl)acetyl}amino]pyridin-4-yl}methyl]oxy}pyridin-2-yl]piperazine-1-carboxamide	
172	N-(3-ethylphenyl)-4-[4-{[(2-{[(4-methylpiperazin-1-yl)acetyl}amino]pyridin-4-yl}methyl]oxy}-1,2,5-thiadiazol-3-yl]piperazine-1-carboxamide	
173	N-[3,5-bis(trifluoromethyl)phenyl]-4-[3-{[(2-{[(4-methylpiperazin-1-yl)acetyl}amino]pyridin-4-yl}methyl]oxy}pyridin-2-yl]piperazine-1-carboxamide	
174	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	

Table 4

175	4-[3-({[2-(acetylamino)pyridin-4-yl]methyl}oxy)pyridin-2-yl]-N-(3-ethylphenyl)piperazine-1-carboxamide	
176	4-(3-{[(2-aminopyrimidin-4-yl)methyl}oxy]pyridin-2-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide	
177	2-[4-(3-{[(2-aminopyrimidin-4-yl)methyl}oxy]pyridin-2-yl)piperazin-1-yl]-N-[3,5-bis(trifluoromethyl)phenyl]acetamide	
178	4-(3-{[(2-aminopyrimidin-4-yl)methyl}oxy]pyridin-2-yl)-N-phenylpiperazine-1-carboxamide	
179	4-(3-{[(2-aminopyrimidin-4-yl)methyl}oxy]pyridin-2-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	
180	4-(3-{[(2-aminopyrimidin-4-yl)methyl}oxy]pyridin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	
181	4-(3-{[(2-aminopyrimidin-4-yl)methyl}oxy]pyridin-2-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide	

Table 4

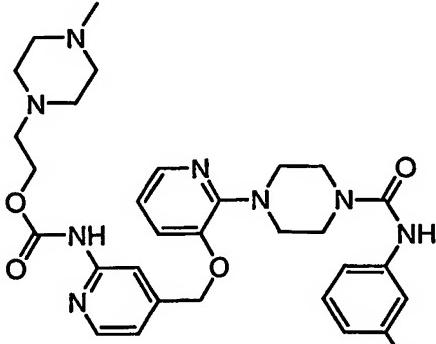
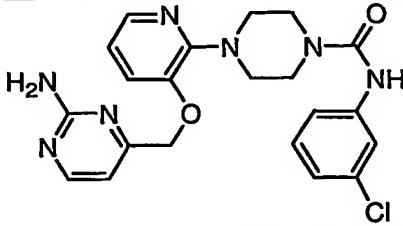
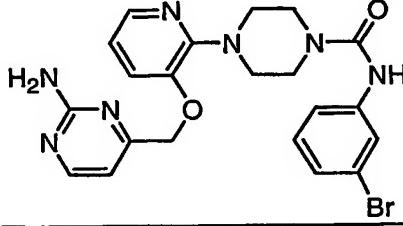
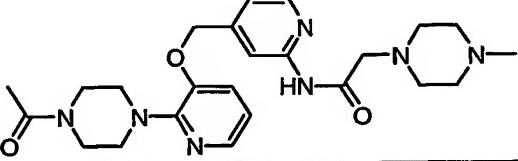
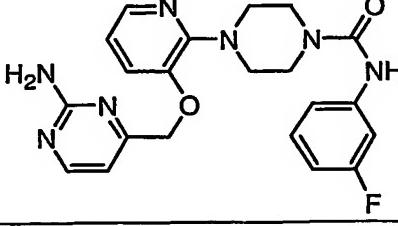
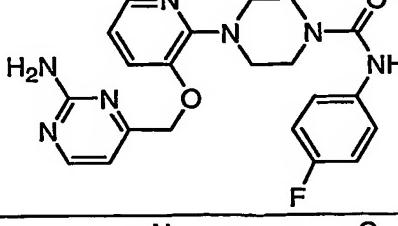
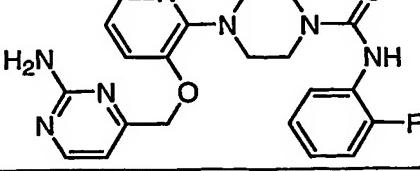
182	2-(4-methylpiperazin-1-yl)ethyl [4-({[2-(4-{[(3-ethylphenyl)amino]carbonyl}piperazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]carbamate	
183	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-chlorophenyl)piperazine-1-carboxamide	
184	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-bromophenyl)piperazine-1-carboxamide	
185	N-[4-({[2-(4-acetyl)piperazin-1-yl)pyridin-3-yl]oxy}methyl)pyridin-2-yl]-2-(4-methylpiperazin-1-yl)acetamide	
186	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-fluorophenyl)piperazine-1-carboxamide	
187	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(4-fluorophenyl)piperazine-1-carboxamide	
188	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(2-fluorophenyl)piperazine-1-carboxamide	

Table 4

189	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	
190	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-5-bromopyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
191	N-methyl-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	
192	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[2-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
193	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(5-chloro-2-fluorophenyl)piperazine-1-carboxamide	
194	4-(3-{[(2-amino-5-bromopyrimidin-4-yl)methyl]oxy}-5-bromopyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
195	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[2-fluoro-3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	

Table 4

196	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
197	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	
198	N-(3-chloro-5-ethylphenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	
199	N-(5-ethyl-2-fluorophenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	
200	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
201	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	

Table 4

202	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	
203	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	
204	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-methylpiperazine-1-carboxamide	
205	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-ethylpiperazine-1-carboxamide	
206	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-cyclohexylpiperazine-1-carboxamide	
207	4-({[2-(4-acetylpirazin-1-yl)pyridin-3-yl]oxy}methyl)pyrimidin-2-amine	
208	4-({[2-(4-propanoylpiperazin-1-yl)pyridin-3-yl]oxy}methyl)pyrimidin-2-amine	
209	N-(3-cyclopropylphenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	

Table 4

210	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-cyclopropylphenyl)piperazine-1-carboxamide	
211	N-[2-fluoro-5-(trifluoromethyl)phenyl]-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	
212	N-[3-fluoro-5-(trifluoromethyl)phenyl]-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	
213	N-(3,5-dichlorophenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	
214	4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-(trifluoromethyl)phenyl)piperazine-1-carboxamide	
215	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	

Table 4

216	4-(3-{[1-(2-aminopyrimidin-4-yl)ethyl]oxy}pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
217	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	
218	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
219	4-[(2-[4-(3,4-dihydroquinolin-1(2H)-ylcarbonyl)piperazin-1-yl]pyridin-3-yl)oxy]methyl)pyrimidin-2-amine	
220	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(2-methylpropyl)piperazine-1-carboxamide	
221	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	
222	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	

Table 4

223	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	
224	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-phenylpiperazine-1-carboxamide	
225	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
226	N-(3,5-diethylphenyl)-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)oxy]methyl}pyridin-2-yl)piperazine-1-carboxamide	
227	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-methylpyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
228	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-methylpyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
229	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	

Table 4

230	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-phenylpiperazine-1-carboxamide	
231	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
232	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
233	N-[3-chloro-5-(trifluoromethyl)phenyl]-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	
234	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
235	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
236	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide	

Table 4

237	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
238	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-bromo-5-ethylphenyl)piperazine-1-carboxamide	
239	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
240	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
241	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide	
242	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	
243	N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]-4-(3-{[(2-{[(4-methylpiperazin-1-yl)acetyl]amino}pyridin-4-yl)methyl]oxy}pyridin-2-yl)piperazine-1-carboxamide	

Table 4

244	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
245	4-(3-{[1-(2-aminopyrimidin-4-yl)ethyl]oxy}pyridin-2-yl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
246	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-chloropyridin-2-yl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	
247	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-(3-ethyl-5-fluorophenyl)piperazine-1-carboxamide	
248	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
249	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3-chloro-2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
250	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyridin-2-yl)-N-[3,5-bis(trifluoromethyl)phenyl]-N-methylpiperazine-1-carboxamide	

Table 4

251	4-(3-{[(2-aminopyrimidin-4-yl)methyl]oxy}pyrazin-2-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide	
252	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-ethyl-4-fluorophenyl)piperazine-1-carboxamide	
253	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-chloro-4-fluorophenyl)piperazine-1-carboxamide	
254	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[2,5-bis(methyloxy)phenyl]piperazine-1-carboxamide	
255	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
256	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3-ethylphenyl)piperazine-1-carboxamide	
257	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(5-chloro-2-fluorophenyl)piperazine-1-carboxamide	
258	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-{3-[(trifluoromethyl)oxy]phenyl}piperazine-1-carboxamide	

Table 4

259	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(methyloxy)phenyl]piperazine-1-carboxamide	
260	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
261	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(1-methylethyl)phenyl]piperazine-1-carboxamide	
262	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[2-chloro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
263	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3-fluorophenyl)piperazine-1-carboxamide	
264	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[2-(ethyloxy)phenyl]piperazine-1-carboxamide	
265	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-(3,4-difluorophenyl)piperazine-1-carboxamide	
266	4-(4-{[(2-aminopyrimidin-4-yl)methyl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3-(methylthio)phenyl]piperazine-1-carboxamide	

Table 4

267	N-(3-acetylphenyl)-4-(4-{{(2-aminopyrimidin-4-yl)methyl}oxy}-1,2,5-thiadiazol-3-yl)piperazine-1-carboxamide	
268	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-[2-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
269	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-(3-fluorophenyl)piperazine-1-carboxamide	
270	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-phenylpiperazine-1-carboxamide	
271	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-(3,5-dichlorophenyl)piperazine-1-carboxamide	
272	4-(2-{{(2-aminopyrimidin-4-yl)methyl}oxy}phenyl)-N-[3-fluoro-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
273	4-[4-({{[6,7-bis(methyloxy)quinolin-4-yl]methyl}oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	

Table 4

274	4-({[4-(4-([3,5-bis(trifluoromethyl)phenyl]acetyl)piperazin-1-yl)-1,2,5-thiadiazol-3-yl]oxy}methyl)pyrimidin-2-amine	
275	5-{{[(2-aminopyrimidin-4-yl)methyl]oxy}-6-[4-({[3,5-bis(trifluoromethyl)phenyl]amino}carbonyl)piperazin-1-yl]pyrazine-2-carboxamide	
276	4-(4-{[6,7-bis(methoxy)quinolin-4-yl]oxy}-1,2,5-thiadiazol-3-yl)-N-[3,5-bis(trifluoromethyl)phenyl]piperazine-1-carboxamide	
277	4-(2-{{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-[3-ethyl-5-(trifluoromethyl)phenyl]piperazine-1-carboxamide	
278	4-(2-{{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(5-ethyl-2-fluorophenyl)piperazine-1-carboxamide	
279	4-(2-{{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3,5-diethylphenyl)piperazine-1-carboxamide	

Table 4

280	4-[({4-[4-(naphthalen-2-ylacetyl)piperazin-1-yl]-1,2,5-thiadiazol-3-yl}oxy)methyl]pyrimidin-2-amine	
281	4-(2-{[(2-aminopyrimidin-4-yl)methyl]oxy}phenyl)-N-(3-chloro-5-ethylphenyl)piperazine-1-carboxamide	

43. A pharmaceutical composition comprising the compound according to any one of claims 1 - 42 and a pharmaceutically acceptable carrier.
44. A metabolite of the compound or the pharmaceutical composition according to any one of claims 1 - 43.
45. A method of modulating the *in vivo* activity of a kinase, the method comprising administering to a subject an effective amount of a composition comprising at least one of the compound according to any of claims 1 - 42 and the pharmaceutical composition according to claim 43.
46. The method according to claim 45, wherein the kinase is Tie-2.
47. The method according to claim 46, wherein modulating the *in vivo* activity of Tie-2 comprises inhibition of Tie-2.
48. A method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of a composition comprising at least one of the compound according to any of claims 1 - 42 and the pharmaceutical composition according to claim 43.
49. A method of screening for modulator of a Tie-2 kinase, the method comprising combining either a composition comprising at least one of the compound according to any of claims 1 - 42 and the pharmaceutical composition according to claim 43, and at least one candidate agent and determining the effect of the candidate agent on the activity of said kinase.

50. A method of inhibiting proliferative activity in a cell, the method comprising administering to said cell an effective amount of at least one of the compound according to any of claims 1 - 42 and the pharmaceutical composition according to claim 43.